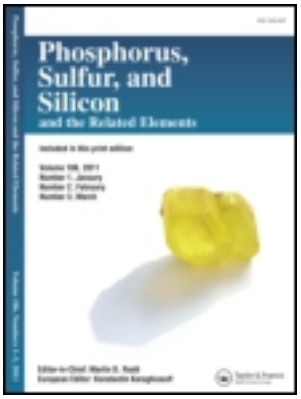

Phosphorus, Sulfur, and Silicon and the Related Elements

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Synthesis of Some New Imidazo[4,5-B]Pyridine Derivatives Using 2-Cyanomethyl-1-Methyl-1H-Imidazo[4,5-B]Pyridine

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SYNTHESIS OF SOME NEW IMIDAZO[4,5-*B*]PYRIDINE DERIVATIVES USING 2-CYANOMETHYL-1-METHYL-1*H*-IMIDAZO[4,5-*B*]PYRIDINE

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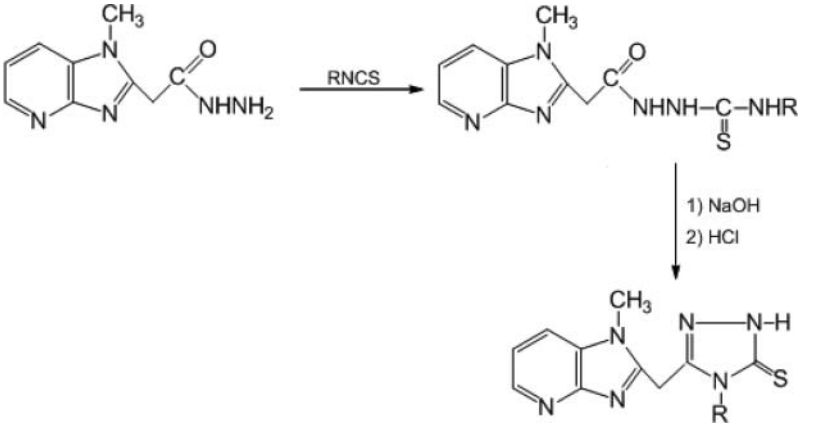
GRAPHICAL ABSTRACT



Abstract *The reactions of 2-cyanomethyl-1-methyl-1H-imidazo[4,5-b]pyridine with isothiocyanates, nitroso compounds, acid chlorides, and thioglycolic acid were investigated. New imidazo[4,5-b]pyridine derivatives with various substituents in 2-position and derivatives of the new pyrrolo[2′,1′:2,3]imidazo[4,5-b]pyridine ring system were synthesized. The compounds obtained were tested in vitro for their tuberculostatic activity.*

Keywords α-Cyanoketones; imidazo[4,5-*b*]pyridine; pyrrolo[2′,1′:2,3]imidazo[4,5-*b*]pyridine; thioamides; tuberculostatic activity

INTRODUCTION

Only a few imidazo[4,5-*b*]pyridine derivatives have been reported; they exhibit diverse bioactivities and some of them have been applied in pharmacotherapy.[1] In continuation of our interest in the chemistry and biological properties of imidazo [4,5-*b*]pyridine derivatives,[2,3] we synthesized and tested some new derivatives of this heterocycle. Previously, we

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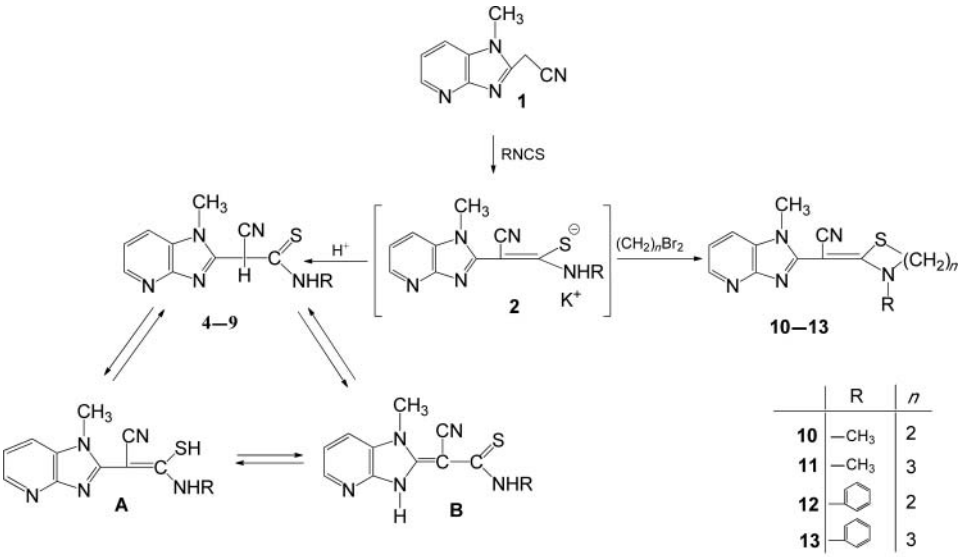
have investigated the reactions of some isothiocyanates with 2-cyanomethylimidazo[4,5-*b*]pyridine and with 2-cyanomethyl-3-methyl-3*H*-imidazo [4,5-*b*]pyridine.[4,5] Since some of carbothioamides obtained there[5] showed a significant activity against *Mycobacterium tuberculosis,* we decided to synthesize isomeric compounds starting from 2-cyanomethyl-1-methyl-1*H*-imidazo[4,5-*b*]pyridine **1** and check whether the position of the CH_3 group in the imidazo[4,5-*b*]pyridine ring has an influence on the tuberculostatic activity. Here, we also describe the synthesis of some new imidazo[4,5-*b*]pyridine derivatives obtained from the reaction of nitrile **1** with some nitroso compounds, acid chlorides, and thioglycolic acid.

RESULTS AND DISCUSSION

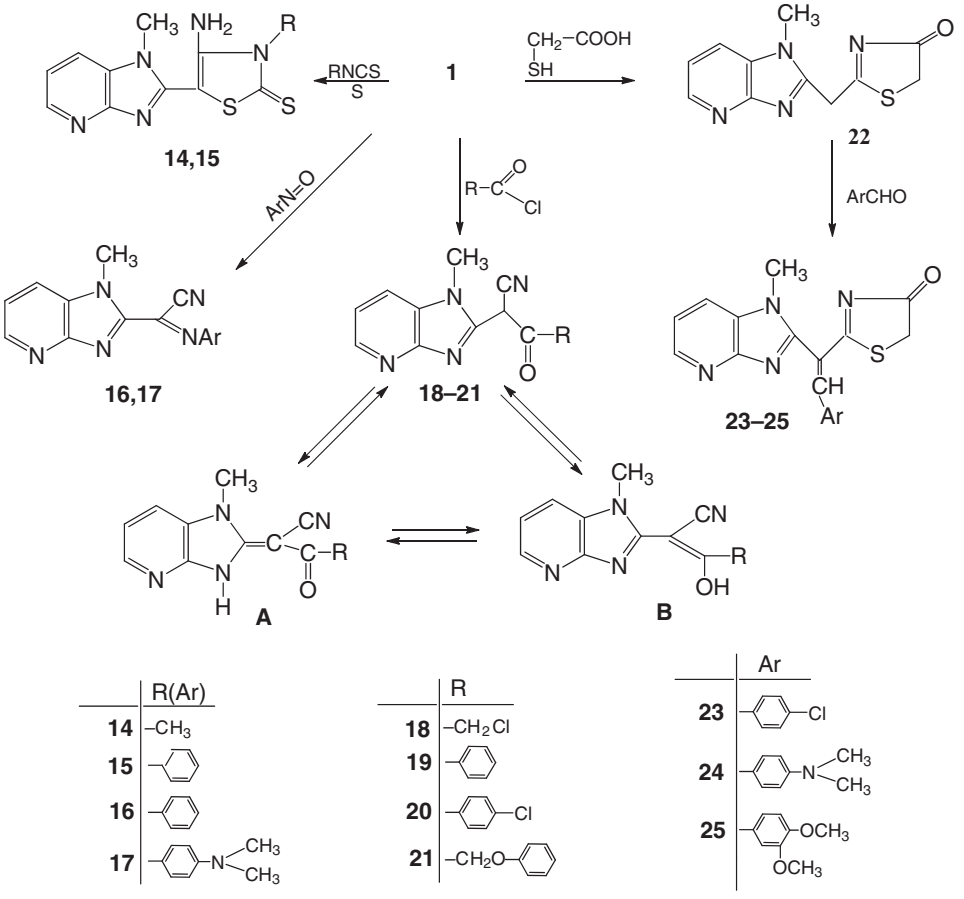
As starting compound for the syntheses the previously reported[6] 2-cyanomethyl-1-methyl-1*H*-imidazo[4,5-*b*]pyridine **1** was used. Reaction of this compound with isothiocyanates in the presence of potassium hydroxide gave the not isolated adduct **2**, which upon acidifying with 1N hydrochloric acid yielded the *N*-substituted thiocarboxamides **4–9**. Reaction of the intermediate **2** with 1,2-dibromoethane or 1,3-dibromopropane gave the compounds **10–13**. When **1** is reacted with methyl- or phenylisothiocyanate in the presence of sulfur the thiazolyl-imidazo[4,5-*b*]pyri-dines **14** and **15** are obtained.

Unexpectedly, the IR spectra of compounds **4–9** showed the presence of a conjugated nitrile group, $\upsilon = 2180\ cm^{-1}$, which suggested that these compounds may exist in two tautomeric forms **A** or **B** (thiol or thione form, Scheme 1). This fact was also suggested by the ^1H NMR spectra of these compounds, in which no signal for a methine proton (CH—CN) was observed. The absence of this signal also confirmed the complete conversion of compounds **4–9** into the isomers **A** or **B** (or a mixture thereof). As in the ^{13}C NMR spectrum of compound **4**, a signal at 189.0 ppm was observed (which is typical for a thione carbon atom[7,8]), it can be concluded that compounds **4–9** exist in the thione form **B**.



4: R = CH_3; **5**: R = CH_2—C_6H_5; **6**: R = C_6H_5; **7**: R = *p*—$CH_3C_6H_4$;
8: R = *p*—ClC_6H_4; **9**: R = C_6H_{11}

Scheme 1



Scheme 2

We also investigated the reactions of nitrile **1** with some nitroso compounds, with some acid chlorides as well as with thioglycolic acid (Scheme 2). From these reactions the enamines **16** and **17**, the α-cyanoketones **18–21** and the thiazolo-imidazo[4,5-*b*]pyridine **22** were obtained. Utilizing the reactivity of the $-CH_2-$ group of compound **22** in reactions with some aromatic aldehydes (*p*-chlorobenzaldehyde, *p-N,N*-dimethylaminobenzaldehyde, 3,4-dimethoxy-benz-aldehyde), the compounds **23–25** were synthesized.

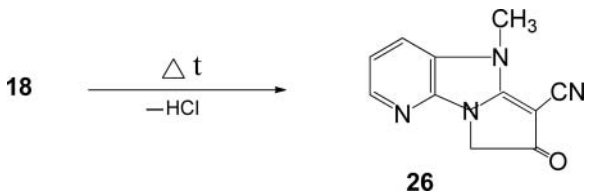
The IR spectra of compounds **18–21** show the presence of a band at 2180 cm^{-1} characteristic for a conjugated nitrile group, which suggests that these compounds may exist in two tautomeric forms **A** or **B**. This possibility was also supported by the ^1H NMR spectra of these compounds, in which no signal for the methine proton (CH—CN) was observed. The absence of this signal also confirmed the complete conversion of compounds **18–21** into the isomers **A** or **B** (or a mixture thereof). Due to the presence of a signal for an >NH proton at about 13 ppm, it may be concluded that compounds **18–21** have in fact the structure **A**. In addition, the ^{13}C NMR spectrum of compound **18** shows a signal at 185.1 ppm typical of a carbonyl carbon atom[8] thus also confirming the structure **A**.

While determining the melting point of compound **18**, a vigorous decomposition was observed at about 225 °C. Subsequently, the sample was recrystallized and melted again

Table 1 ^{1}H and ^{13}C NMR data of some of the new compounds

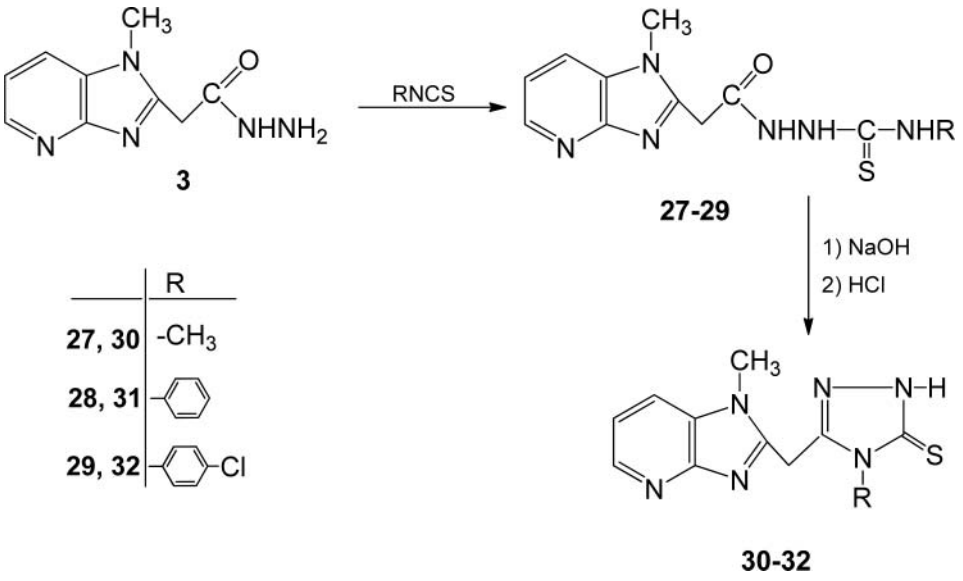
	Solvent	δ (ppm), J (Hz)
4	$CDCl_3$	3.26 (d, $J = 4.7$, 3H, $NHCH_3$), 4.00 (s, 3H, NCH_3), 7.24 (m, 1H, C(6)H), 7.51 (d, $J = 8.2$, 1H, C(7)H), 8.3 (d, $J = 5.0$, 1H, C(5)H) ^{13}C NMR: 32.6, 32.7, 64.7, 116.3, 119.0, 120.6, 126.0, 143.4, 144.7, 153.6, 189.0
10	$CDCl_3$	3.36 (d, $J = 4.8$, 4H, $(CH_2)_2$), 3.49 (s, 3H, NCH_3), 3.87 (s, 3H, NCH_3), 7.14 (dd, $J_1 = 4.8$, $J_2 = 7.0$, 1H, C(6)H), 7.38 (d, $J = 6.7$, 1H, C(7)H), 8.40 (d, $J = 3.6$, 1H, C(5)H)
14	DMSO-d_6	3.68 (s, 3H, NCH_3), 3.82 (s, 3H, NCH_3), 7.19 (dd, $J_1 = 4.8$, $J_2 = 5.4$, 1H, C(6)H), 7.94 (d, $J = 7.8$, 1H, C(7)H), 8.01 (s, 2H, NH_2), 8.30 (d, $J = 4.4$, 1H, C(5)H)
16	DMSO-d_6	4.16 (s, 3H, NCH_3), 7.41 (m, 3H, Ar—H), 7.49 (dd, $J_1 = 5.8$, $J_2 = 4.4$, 1H, C(6)H), 7.57 (t, $J = 7.8$, 2H, Ar—H), 8.27 (d, $J = 7.8$, 1H, C(7)H), 8.62 (d, $J = 5$, 1H, C(5)H)
18	DMSO-d_6	3.94 (s, 3H, NCH_3), 4.50 (s, 2H, CH_2Cl), 7.42 (dd, $J_1 = 5.4$, $J_2 = 7.8$, 1H, C(6)H), 8.19 (d, $J = 8.3$, 1H, C(7)H), 8.36 (d, $J = 4.3$, 1H, C(5)H), 13.45 (s, 1H, NH) ^{13}C NMR: 32.2, 46.5, 64.3, 119.0, 119.6, 120.1, 125.7, 143.1, 144.6, 185.1
22	DMSO-d_6	3.69 (s, 3H, NCH_3), 3.85 (s, 2H, $-CH_2-$), 6.14 (s, 2H, $-CH_2-$), 7.12 (dd, $J_1 = 5.3$, $J_2 = 7.8$, 1H, C(6)H), 7.83 (d, $J = 7.8$, 1H, C(7)H), 8.25 (d, $J = 4.4$, 1H, C(5)H)
23	DMSO-d_6	3.78 (s, 3H, NCH_3), 6.40 (s, 1H, CH), 7.20 (dd, $J_1 = 4.8$, $J_2 = 4.7$, 1H, C(6)H), 7.53 (s, 1H, CH), 7.75 (m, 4H, Ar—H), 7.95 (d, $J = 1.3$, 1H, C(7)H), 8.31 (d, $J = 1.3$, 1H, C(5)H), 12.2 (br s, 1H, Ar—OH)
26	DMSO-d_6	3.85 (s, 3H, CH_3), 4.52 (s, 2H, CH_2), 7.33 (dd, $J_1 = 5$, $J_2 = 7$, 1H, C(3)H), 8.04 (d, $J = 7$. 1H, C(4)H), 8.23 (d, $J = 5$, 1H, C(2)H)
30	DMSO-d_6	3.45 (s, 3H, NCH_3), 3.86 (s, 3H, NCH_3), 4.62 (s, 2H, CH_2), 7.28 (dd, $J_1 = 4.7$, $J_2 = 8.1$H, C(6)H), 8.03 (d, $J = 7$, 1H, C(7)H), 8.38 (d, $J = 6$, 1H, C(5)H)

at about 320 °C. This observation suggested the possibility of a cyclization. This was confirmed experimentally: a sample of compound **18** was heated at 250 °C for about 5 min (until the decomposition was complete) and the product obtained after cooling was recrystallized and investigated. Based on the IR, ^{1}H NMR, and MS spectra, we established that compound **18** loses a molecule of HCl at its melting temperature and undergoes intramolecular cyclization to yield a new heterocyclic system, pyrrolo[2′,1′: 2,3]imidazo[4,5-*b*]pyridine **26** (Scheme 3). It is worth to note that according to ^{1}H NMR data compound **23** exists in the isomeric enole form (Table 1).



Scheme 3

In a further set of experiments, reaction of hydrazide **3** with methyl-, phenyl-, or *p*-chlorophenyl isothiocyanate yielded the corresponding acyl-thiosemicarbazides **27–29**. Their cyclization in alkaline medium allowed us to prepare the 1,2,4-triazole derivatives **30–32**.



Scheme 4

MICROBIOLOGY

The new compounds were tested in vitro for their tuberculostatic activity against *Mycobacterium tuberculosis* $H_{37}Rv$ and two "wild" strains isolated from tuberculotic patients: the 210 strain resistant to isoniazide (INH), *p*-aminosalicylic acid (PAS), ethambutol (ETB), and rifampicine (RFP) as well as the 192 strain, fully susceptible to the drugs administered. The investigations were performed by a classical test-tube method of successive dilution with Youman's liquid medium containing 10% of bovine serum.[3] The determined minimum concentrations inhibiting the growth of tuberculous strains (MIC) for all the tested compounds were within the limits 50–100 μg/mL, which indicates low tuberculostatic activity. These results show that CH_3 group in position **1** of the imidazopyridine ring does not increase the tuberculostatic activity of the obtained compounds.

EXPERIMENTAL

Melting points were determinated with a Reichert apparatus and are uncorrected. IR spectra: Termo Nicolet Satelite FT IR spectrophotometer (pellets in KBr). ^{1}H and ^{13}C NMR: Varian Gemini 200 spectrometer (200 MHz for ^{1}H, 50 MHz for ^{13}C) with TMS as an internal standard; chemical shifts δ in ppm. MS spectra: Varian Mat 711 apparatus with direct inlet; ionization energy 70 eV. The results of elemental analyses (C, H, N) for all new compounds obtained were in agreement with the calculated values $\pm$ 0.4%. Physical and spectral data of the synthesized compounds are given in Tables 1 and 2.

2-[(*N*-Substituted thiocarbamoyl) cyanomethyl]-1-methyl-1*H*-imidazo[4,5-*b*]pyridines (4–9): General Procedure

To a suspension of finely powdered KOH (5 mmol) in dry DMF (15 mL) at 0 °C, the nitrile **1**[6] (5 mmol) and then the appropriate isothiocyanate (5 mmol) were added in

Table 2 Characteristics of the new compounds **4–32**

	mp (°C) solvent	Yield (%)	Formula mol. wt.	IR (cm^{-1})	MS [*m/z* (I,%)]
4	210–212 toluene	74	$C_{11}H_{11}N_5S$ 245.30	3317, 2928, 2180, 1567, 1280	M^+ 245(96), 215(6), 213(18), 212(100), 198(5), 197(26), 183(7), 172(7), 171(7), 157(8), 78(7)
5	204–206 toluene	80	$C_{17}H_{15}N_5S$ 321.33	3310, 3029, 2939, 2183, 1575, 1522, 1278	M^+ 321(93), 288(22), 215(13), 183(19), 172(12), 92(9), 91(100)
6	191–193 DMF/H_2O	78	$C_{16}H_{13}N_5S$ 307.33	3349, 3020, 2947, 2180, 1569, 1236	M^+ 307(3), 173(11), 172(100), 171(10), 157(10), 135(41), 132(18), 105(20), 79(32), 78(13), 52(21), 39(10), 28(27)
7	214–215 DMF	81	$C_{17}H_{15}N_5S$ 321.33	3320, 3060, 2910, 2180, 1520, 1090	M^+ 321(6), 288(10), 173(10), 172(97), 171(12), 157(14), 150(10), 149(100), 148(30), 132(19), 107(12), 106(14), 105(26), 91(72), 78(17)
8	208–210 toluene	72	$C_{16}H_{12}ClN_5S$341.78	3166, 3040, 2947, 2179, 1560, 1138	M^+ 341(16), 308(27), 172(95), 171(43), 169(100), 132(18), 111(32), 105(18), 79(21), 75(18)
9	203–205 DMF/H_2O	73	$C_{16}H_{19}N_5S$ 313.35	3310, 2910, 2840, 2180, 1570, 1130	M^+ 313(70), 258(24), 215(18), 199(16), 198(100), 183(16), 171(13), 98(15), 78(17), 45(5)
10	216–218 DMF/H_2O	65	$C_{13}H_{13}N_5S$ 271.33	2960, 2900, 2220, 1610	M^+ 271(75), 247(25), 246(100), 242(23), 215(39), 213(80), 210(34), 183(58), 172(51), 171(60), 170(36), 157(88), 132(51), 105(48), 103(43), 91(36), 78(97), 64(43), 60(52), 52(59)
11	225–226 benzene	59	$C_{14}H_{15}N_5S$ 285.36	2940, 2870, 2220, 1600	M^+ 285(77), 255(30), 246(95), 243(84), 215(57), 209(24), 203(27), 198(76), 184(74), 182(30), 172(75), 171(70), 157(100), 132(50), 105(60), 91(50), 78(94), 64(61), 52(75), 41(70)
12	168–170 benzene	30	$C_{18}H_{15}N_5S$ 333.40	2925, 2184, 1612	M^+ 333(100), 305(27), 287(9), 286(36), 278(8), 273(22), 272(9), 259(10), 233(8), 172(8), 135(9), 104(8), 91(12), 79(12), 78(28), 77(32), 52(13), 51(23), 43(12), 39(14)
13	234–236 benzene	31	$C_{19}H_{17}N_5S$ 347.43	2939, 2190, 1591	M^+ 347(34), 291(13), 288(27), 286(12), 275(93), 241(36), 214(18), 172(66), 157(10), 135(100), 132(15), 105(26), 93(49), 78(54), 66(19), 52(31), 51(64), 41(25), 39(34)
14	312–315 DMF	43	$C_{11}H_{11}N_5S_2$ 277.36	3300, 3263, 3054, 2940, 1632, 1610, 1109, 769	M^+ 277(36), 204(7), 178(4), 177(38), 176(21), 133(4), 78(5), 45(5), 44(100), 43(7), 41(6), 39(5), 37(7)
15	265–268 DMF/H_2O	52	$C_{16}H_{13}N_5S_2$ 339.44	3308, 3243, 3054, 2920, 1630, 1612, 1134, 770	M^+ 339(71), 212(5), 204(27), 178(11), 177(100), 176(44), 135(15), 133(8), 132(6), 103(6), 78(11), 45(5), 77(18), 51(12), 44(37), 43(5), 39(6)
16	193–196 EtOH	73	$C_{15}H_{11}N_5$ 261.27	3052, 2232, 1612	M^+ 261(42), 260(100), 246(13), 245(7), 194(3), 77(8), 51(4)

17	290–293 DMF	84	$C_{17}H_{16}N_5$ 304.34	2918, 2204, 1613	M^+ 304(61), 303(100), 289(12), 288(7), 287(9), 275(5), 273(4), 261(4), 260(17), 251(6), 237(4), 152(5), 151(4)
18	223–225 EtOH/Dioxane	42	$C_{11}H_9ClN_4O_2$ 48.67	3064, 2966, 2937, 2188, 1614, 1531, 798	M^+ 248(35), 250(12), 200(21), 199(100), 171(16), 103(9), 93(9), 78(19), 52(11), 51(12), 39(10)
19	220–222 EtOH/Dioxane	37	$C_{16}H_{12}N_4O$ 276.30	3054, 2924, 2194, 1619, 1590	M^+ 276(61), 275(100), 199(10), 105(28), 78(14), 77(51), 51(17)
20	245–247 DMF/H_2O	34	$C_{16}H_{11}ClN_4O$ 310.74	3086, 2922, 2202, 1684, 1583, 794	M^+ 310(55), 312(19), 309(100), 308(10), 199(22), 171(10), 141(19), 139(43), 113(15), 111(49), 103(10), 78(21), 75(23), 52(13), 51(18), 50(10), 39(14)
21	190–192 EtOH/Dioxane	45	$C_{17}H_{14}N_4O_2$ 306.33	3052, 2922, 2188, 1634, 1551, 1232, 1158, 760	M^+ 306(24), 200(24), 199(100), 185(22), 171(11), 93(9), 78(18), 77(16), 51(14), 39(14)
22	294 (dec.) DMF	76	$C_{11}H_{10}N_4OS$ 246.28	2937, 1707, 1621	M^+ 246(100), 213(6), 173(11), 172(46), 158(5), 132(20), 78(6), 69(5), 57(8), 55(6), 44(9), 43(7)
23	343–345 DMF	64	$C_{18}H_{13}ClN_4OS$ 368.85	3050, 2920, 1696, 1606	M^+ 368(25), 370(11), 173(14), 172(100), 171(10), 168(7), 167(4), 133(4), 132(16), 89(4), 78(4)
24	321–325 DMF	78	$C_{20}H_{19}N_5OS$ 377.47	3051, 2917, 1687, 1621	M^+ 377(20), 178(15), 177(100), 176(24), 172(4), 161(5), 132(4), 42(4)
25	303–306 DMF	67	$C_{20}H_{18}N_4O_3S$ 394.45	3011, 2954, 1699, 1622, 1158	M^+ 394(34), 223(7), 196(7), 195(22), 194(100), 193(6), 179(27), 173(9), 172(41), 171(5), 151(5), 132(13), 107(7), 78(5)
26	320–324 DMF/H_2O	82	$C_{11}H_8N_4O$ 212.20	2923, 2202, 1601	M^+ 212(100), 183(27), 172(14), 158(8), 144(11), 105(8), 79(13), 78(16), 52(16), 51(15), 39(14)
27	217–220 not cryst.	80	$C_{11}H_{14}N_6OS$ 278.34	3313, 2942, 1681, 1543, 1410, 1216, 1055	
28	227–229 not cryst.	82	$C_{16}H_{16}N_6OS$ 340.40	3284, 3032, 2920, 1688, 1569, 1497, 1365, 1209	
29	207–209 not cryst.	71	$C_{16}H_{15}ClN_6OS$ 374.85	3253, 3035, 2930, 1679, 1618, 1411, 1329, 1091, 776	
30	315–318 DMF/H_2O	80	$C_{11}H_{12}N_6S$ 260.32	3448, 3067, 2854, 2695, 1617, 1506, 1475, 1309, 1085	M^+ 260(100), 259(12), 214(17), 173(39), 172(12), 147(23), 146(72), 133(17), 132(20), 78(12), 52(12), 42(12)
31	313–316 DMF/H_2O	81	$C_{16}H_{14}N_6S$ 322.39	3432, 3036, 2884, 2749, 1612, 1572, 1498, 1320, 1013	M^+ 322(100), 321(16), 249(16), 223(19), 222(28), 173(31), 172(15), 146(36), 132(30), 91(12), 78(24), 77(19), 51(28), 39(20)
32	318–321 DMF/H_2O	78	$C_{16}H_{13}ClN_6S$ 356.83	3447, 3021, 2933, 2841, 1500, 1411, 1285, 1092	M^+ 356(100), 257(15), 256(20), 173(34), 172(17), 147(16), 146(43), 132(40), 105(12), 78(25), 52(24), 39(20)

portions with stirring. The reaction mixture was stirred at room temperature for 3 h, then poured into ice/water (150 mL) and acidified with 0.1 N HCl to pH 3–4. The resulting precipitate was filtered off, dried, and recrystallized from the proper solvent (Table 2).

1-Methyl-1*H*-imidazo[4,5-*b*]pyridines (10–13): General Procedure

To a cooled (0 °C) suspension of finely powdered KOH (5 mmol) in dry DMF (15 mL), the nitrile **1**[6] (5 mmol) and then methyl- or phenylisothiocyanate (5 mmol) were added in portions with stirring. The reaction mixture was stirred at room temperature for 3 h, then cooled again to 0 °C, treated with the appropriate dibromoalkane (5 mmol), and stirred at room temperature for additional 3–5 h. After that time, the reaction mixture was poured into ice/water (150 mL), the resulting product was filtered off, dried, and recrystallized from the proper solvent (Table 2).

1-Methyl-1*H*-imidazo[4,5-*b*]pyridines (14,15): General Procedure

A mixture of nitrile **1**[6] (5 mmol), finely powdered sulfur (5 mmol), and triethylamine (5 mmol) in abs. EtOH (15 mL) was stirred at room temperature for 30 min. The proper isothiocyanate (5 mmol) was then added gradually and stirring was continued for 20 min. Next, the reaction mixture was refluxed with constant stirring for 2 h. After cooling, the resulting precipitate was filtered off, washed with ether (2 × 3 mL), dried, and recrystallized (Table 2).

2-(1-Methyl-1*H*-imidazo[4,5-*b*]pyridine-2-yl) Acetonitriles (16,17): General Procedure

A mixture of nitrile **1**[6] (2 mmol), nitrosobenzene or 4-nitroso-*N,N*-dimethylaniline (3 mmol), and piperidine (0,3 mL) in absolute ethanol (10 mL) was stirred at room temperature for 4–5 h. The resulting solid was filtered off and recrystallized (Table 2).

Synthesis of Compounds 18–21: General Procedure

A cooled (0 °C–2 °C) suspension of finely powdered KOH (2 mmol) in dry DMF (10 mL) and nitrile **1**[6] (2 mmol) was stirred for 30 min. Then a cooled solution of the appropriate acid chloride (2 mmol) in DMF (1 mL) was added dropwise and stirring was continued for 1 h. After that time, the reaction mixture was further stirred at room temperature for 2 h, and then, poured into ice/water (100 mL). The resulting precipitate was filtered off, dried, and recrystallized (Table 2).

2-[(1-Methyl-1*H*-imidazo[4,5-*b*]pyridin-2-yl)methyl]-1,3-thiazol-4(5*H*)-one (22)

Nitrile **1**[6] (0.52 g, 3 mmol), thioglycolic acid (0.21 mL, 3 mmol), and phenyl ether (0.5 g) were heated with stirring at 175 °C–180 °C for 8 min. The solid obtained after cooling was washed with ether (2 × 5 mL) and recrystallized (Table 2).

Synthesis of 1,3-Thiazol-4(5*H*)-ones (23–25): General Procedure

To a suspension of compound **22** (2 mmol) and the appropriate aldehyde (2.5 mmol) in anhydrous ethanol (10 mL), 0.3 mL of piperidine was added and the mixture was refluxed with stirring for 3 h. The solid precipitated after cooling was filtered off and recrystallized (Table 2).

5-Methyl-7-oxo-7,8-dihydro-5*H*-pyrrolo[2′,1′:2,3]imidazo[4,5-*b*]pyridine-6-carbonitrile (26)

Powdered compound **18** (0.5 g) was heated with stirring at 250 °C for about 5 min (until HCl evolution was complete). The solid obtained after cooling was washed with ether (2 × 3 mL) and recrystallized (Table 2).

1-(1-Methyl-1*H*-imidazo[4,5-*b*]pyridin-2-yl-acetyl)-4-substituted Thiosemicarbazides (27–29): General Procedure

To a solution of compound **3**[6] (1.5 mmol) in methanol or anhydrous benzene (10 mL), the appropriate isothiocyanate (1,6 mmol) was added and the reaction mixture was refluxed with stirring for 3 h. The solid precipitated after cooling was filtered off and dried (Table 2).

2,4-Dihydro-3*H*-1,2,4-triazol-3-thiones (30–32): General Procedure

A solution of the appropriate thiosemicarbazide (**27–29**) (2 mmol) in 4% aqueous NaOH (6 mL) was refluxed for 1–2 h. Then the reaction mixture was cooled and acidified with 15% aqueous HCl to a pH of 3–4. The resulting precipitate was filtered off, dried, and recrystallized (Table 2).

REFERENCES

1. Negver, M. *Organic-Chemical Drugs and Their Synonyms*, Vols. 1–4, 7th ed.; Academie-Verlag: Berlin, **1994**.
2. Bukowski, L. *Chem. Heterocycl. Comp.* **2002,** 38, 828–835.
3. Bukowski, L.; Janowiec, M.; Zwolska, Z.; Andrzejczyk, Z. *Pharmazie* **1999,** 54, 651–654.
4. Bukowski, L.; Janowiec, M.; Zwolska-Kwiek, Z.; Andrzejczyk, Z. *Pharmazie* **1998,** 53, 373–376.
5. Bukowski, L. *Pharmazie* **2001,** 56, 23–27.
6. Bukowski L.; Janowiec, M. *Pharmazie* **1990,** 45, 904–907.
7. Cho, N. S.; Kim, Q. N.; Parkanyi, C. *J. Heterocycl. Chem.* **1993,** 30, 397–401.
8. Breitmaier E.; Voelter, W. *Carbon-13 NMR Spectroscopy*, 3rd ed.; Verlag Chemie: Weinheim, **1987**.